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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,592	10/09/2001	Robert G. Korneluk	07891/009004	8174

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EXAMINER	
EPPS, JANET L	

ART UNIT	PAPER NUMBER
1635	13

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,952	CHOU ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 9-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 9-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Listing

2. The specification as filed, at page 67, line 7, refers to SEQ ID NO: 1-42, this statement is inconsistent with the Sequence Listing of record in the application, which only lists a total of 17 sequences, SEQ ID NO: 1-17.

Response to Amendment

3. The Declaration under 37 CFR 1.132 filed 5-22-03 is insufficient to overcome the rejection of claims 5 and 9-15 based upon 35 USC § 112, 1st paragraph as set forth in the last Office action because: the showing of the Korneluk Declaration is not commensurate in scope with the claims, for further discussion see response set forth below.

Response to Arguments

4. Claims 5 and 9-15 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the claimed method *in vitro*, and *in vivo* comprising administering phosphorothioate modified antisense oligonucleotides that are 19 nucleotides in length, does not reasonably provide enablement for the *in vivo* therapeutic treatment of a patient comprising administration of unmodified antisense oligonucleotides of any other length. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons of record as set forth in the Official Action mailed 11-20-02.

5. Applicant's arguments filed 5-22-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that undue experimentation would not be required to practice the claimed invention since the Declaration of Dr. Robert Korneluk provides evidence of the sufficiency of Applicant's disclosure. Applicants argue that the Declaration of Korneluk shows that Applicants have reduced to practice the present invention using techniques known to those skilled in the art of antisense oligonucleotide technology at the time of filing. However, the results obtained in the Korneluk Declaration were obtained using antisense oligonucleotides that were not previously described in the specification as originally filed. The specification as filed, and claims, do not describe the 96 antisense oligonucleotides targeting XIAP that are described in the Declaration of Korneluk. Applicants have under taken further experimentation to demonstrate the efficacy of two antisense oligonucleotides, G4 and F3. However, there are multiple antisense oligonucleotides that are encompassed by the instant claims, i.e. that meet the structural requirements of the instant claim, namely wherein said antisense oligonucleotide is of length sufficient to inhibit an inhibitor of apoptosis, and where said antisense nucleic acid is complementary to a portion of human X-linked IAP. Moreover, it is noted that the methods recited in the instant claims are not limited to the phosphorothioate modified antisense oligonucleotides of 19 nucleotides in length that are described in the Korneluk Declaration as being capable of use in the *in vivo* methods according to the present invention. The instant claims merely state that the antisense nucleic acids used in the claimed methods are of length sufficient to inhibit and are complementary to a portion of human XIAP, however Applicant's results indicate that mere length and complementarity of the antisense oligonucleotide is not sufficient to result in inhibition of an inhibitor of apoptosis, since for

example antisense oligonucleotides G3 and G4 are of the same length and are both complementary to XIAP mRNA, however G3 does not down regulate XIAP expression, and the G4 oligonucleotide does inhibit (See Table 1 in Exhibit A).

The Declaration of Korneluk does not demonstrate the effective delivery of antisense nucleic acid of any length and/or modification, wherein delivery of the antisense nucleic acid results in the treatment of a patient diagnosed with a proliferative disease.

Moreover, as stated in the prior Office Action, Chirila et al. (2002), Jen et al. (2000), and Stein (2000) teach that the behavior of oligonucleotide based compositions and their delivery *in vivo* are unpredictable, therefore claims to pharmaceutical compositions and methods of treating diseases by the administration of oligonucleotide based pharmaceuticals are subject to the question of enablement due to the high level of unpredictability associated with this technique as taught in the prior art.

Therefore, the specification does not describe the use of full scope of antisense oligonucleotides encompassed by the instant claims as an inhibitor of IAP for the *in vivo* treatment of a disease or condition associated with the expression of *XIAP,* in a sufficient manner so as to enable one of ordinary skill in the art to practice the full scope of the present invention without undue experimentation. This conclusion is based upon the known unpredictability regarding the delivery of antisense *in vivo,* the behavior of an antisense compound in a cell, the production of secondary treatment effects of diseases or conditions associated with the expression of *XIAP* in a patient, and the lack of guidance in the specification as filed in this regard.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on Monday-Thursday, 8:30 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
August 6, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635